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WO 94/07470 A

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(54) Abstract Title
Injection-moulded capsules

(57) A capsule is made by injection-moulding from one or more of a range of thermoplastic materials, typically a soluble polyvinylalcohol, and is constructed to dissolve at varying rates in an aqueous environment.

The capsule may have raised or incuse portions moulded into its external surface, which patterns may define a code or simply be rib-like, to assist in its partial dissolution.

The injection-mouldable material can contain one or more particulate solid in order to accelerate the rate of dissolution of the capsule.

It can also be made from materials that will not hold a static charge.

The capsule is for delivering into an aqueous environment substances such as detergents, pesticides, biocides, deodorants, dyes and pigments, and water-treatment chemicals.

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At least one drawing originally filed was informal and the print reproduced here is taken from a later filed formal copy.

The claims were filed later than the filing date but within the period prescribed by Rule 25(1) of the Patents Rules 1995.

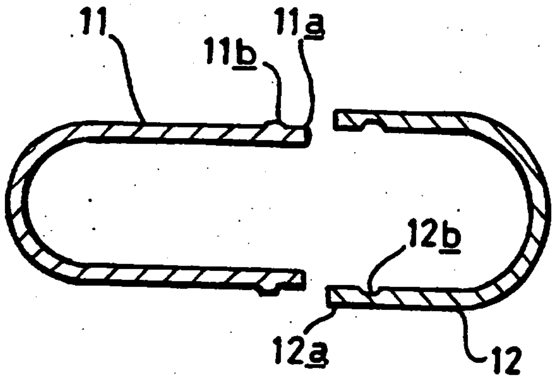

Fig. 1A

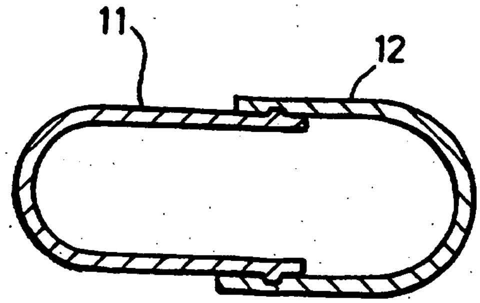

Fig. 1B

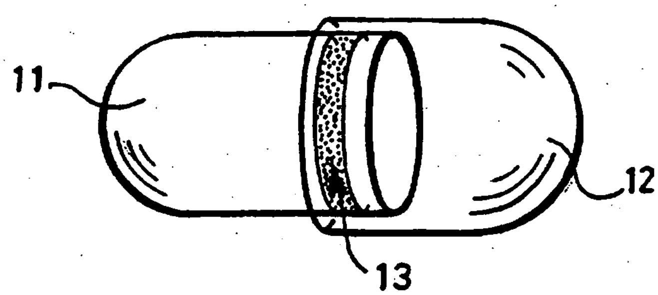

Fig. 2

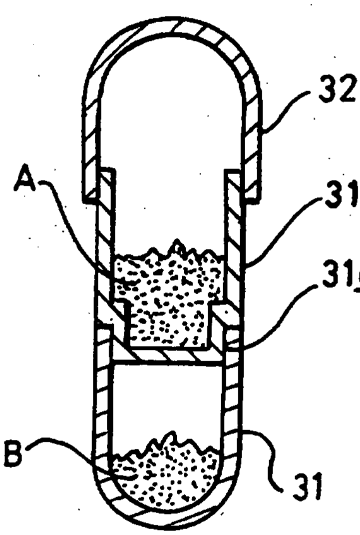

Fig. 3A

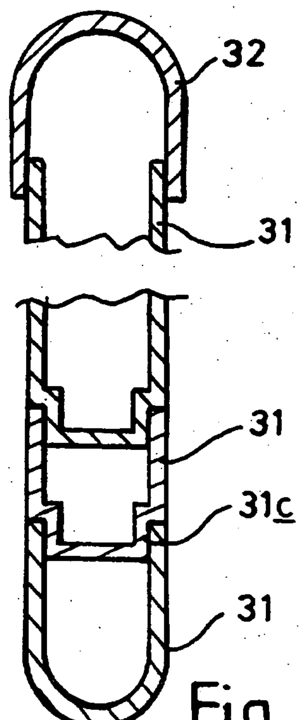

Fig. 3B

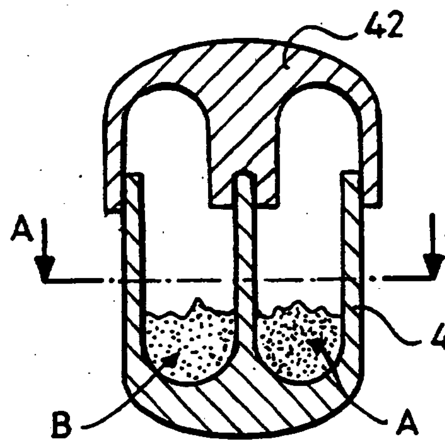

Fig. 4A

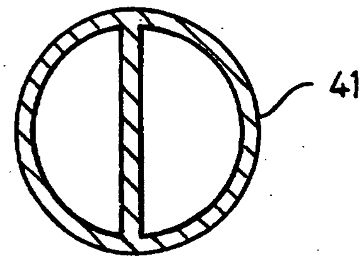

Fig. 4B

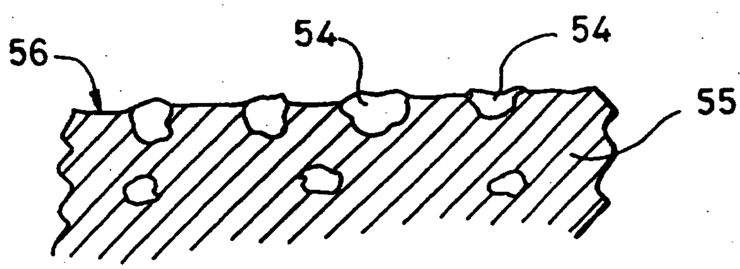

Fig. 5

Fig. 6A

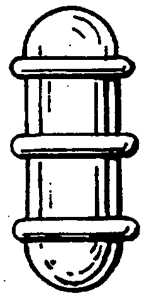

Fig. 6B

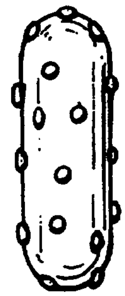

Fig. 6C

Fig. 6D

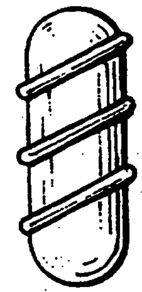

Fig. 6E

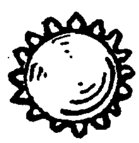

Fig. 6F

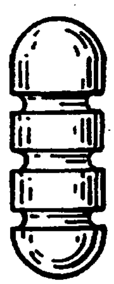

Fig. 6G

Fig. 6H

Fig. 6I

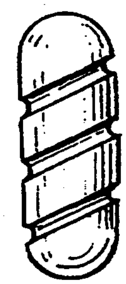

Fig. 6J

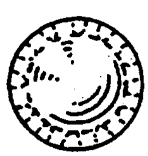

Fig. 6K

Fig. 6L

Fig. 6M

Capsule-like containers

This invention is concerned with capsule-like containers, and relates in particular to such containers that may be utilised for the delivery into an aqueous environment of substances such as detergents, pesticides, biocides, deodorants, dyes and pigments, and water-treatment chemicals.

In the Specification of our co-pending Patent Application No: 99/27,144.7 (Publication No: ?,???,???) (P1581) there is described a novel form of capsule useful for the delivery of medical preparations into the Patient. More particularly, there is described, as a replacement for the hard gelatine capsules commonly in use, a novel form of capsule which is injection-moulded and will at least in part dissolve in the body. It has now been appreciated that this type of capsule - one that is injection-moulded, and can at least in part dissolve at the intended use site - has utilisations other than in medicine and the human or animal body. In particular, it has been realised that many substances that must be packaged for delivery to their use site could, where that site is an aqueous environment, be contained in similar, though somewhat larger, capsules. Thus, a capsule-like container - a "capsular" container - could be employed to deliver, for example, detergents to a washing machine, pesticides to a paddy field, or water-treatment chemicals to a reservoir.

In one aspect, therefore, this invention provides a relatively large capsular container that may be utilised

for the delivery of some water-destined ingredient, which capsular container is made of a material that can be injection-moulded and will at least in part dissolve in the intended aqueous destination site.

As discussed further below, the capsular container of the invention will, unless otherwise designed, fully dissolve in the intended aqueous destination site. In so doing, it will release its contents over a desired period of time.

Apart from its size - the capsular container of the invention is relatively larger - the capsular container is very like the capsule of the aforementioned Specification, *mutatis mutandis*. Briefly, though, it may be described as follows:-

The invention provides a capsule - that is to say, a container for the relevant ingredients, which container is in at least two parts (a body part and a cap part) which fit tightly, and preferably sealingly and inseparably, together to form a compartment in which is stored the ingredient to be delivered. In one example, the capsule may have three parts - a body, a first cap, and then a second cap to fit over the closed end of either the body or the first cap, so as to result in a capsule with two separate compartments. And where there are three such parts (or more; four parts - a body and three caps - make three compartments, and so on), then naturally the ingredients in each compartment may be the same or they may be different.

By using capsule cap/body parts of different thicknesses, or of different polymers, or both, this invention enables enhanced control over the release of

different ingredients at different times or in different positions within broad scope of the aqueous destination.

The capsular container is most conveniently of the standard capsule shape - an elongate tubular package with closed, rounded ends - but of course it is relatively larger than the capsule described in the aforementioned Specification. Moreover, although it is possible to have the several parts of much the same sizes, it is usual that there will be a long body with a shorter cap (the cap may be half or a quarter the length of the body). Typically, a capsular container has an overall closed length of 4-10cm (about 2-4in) and an external diameter of 2-4cm (about 0.8-1.7in). However, it should be understood that there is no theoretical limitation, in either size or shape, and what is suitable will normally be decided upon the basis of the "dose" of the container's contents, the size of any aperture the container may have to pass through, and the available means of delivery.

The invention's capsular container is intended to be utilised for the delivery of some ingredient to an aqueous destination. It is clearly necessary that the material from which the capsule is made - the material that can be injection-moulded - should of course be safe for this delivery. PVOH - polyvinylalcohol - is such a material; not only is it non-toxic but it is available in various grades including, where necessary, food-quality grades, and it is very much preferred.

PVOH - or more specifically PVOH-based formulations - is presently the most convenient injection-mouldable, water-soluble or water-dispersible, material, and of the various commercially-available PVOH formulations one particularly-preferred variety is that range of materials

sold (in the form of granules) under the name CP1210T05 by Soltec Developpement SA of Paris, France

In general, PVOH polymers are synthetic materials capable, when appropriately formulated with other adjuvants - such as plasticisers, particularly glycerine (but other glycols and polyglycols may be used), and solids such as talc, stearic acid, magnesium stearate, silicon dioxide, zinc stearate, and colloidal silica - of being moulded at temperatures between 180-220°C, depending upon the formulation selected and the melt flow index required, into capsule bodies and caps of the appropriate hardness, texture and solubility characteristics.

PVOH materials, unlike gelatine, can be modified to dissolve at different rates under varying conditions (including the pH of the aqueous medium into which they are introduced).

The invention provides a capsular container which is in at least two parts (a body part and a cap part) which fit tightly, and preferably sealingly and inseparably, together. The actual joining of the parts can be carried out in any convenient way, but advantage can be taken of the very nature of the capsule material - the fact that it is one that can be injection-moulded (it is a thermoplastic). Thus, the preferred joining method is welding - either heat welding, by melting the parts when they are in contact, and allowing them to "run" into each other and then cool and solidify to become an integral device, or solvent welding, where much the same effect is achieved by partially dissolving the adjacent portions of the capsule and letting them again run into each other and then solidify to form a whole. Heat welding is much the preferred way.

Indeed, in one of its several aspects the invention specifically provides an injection-moulded capsular container having a cap portion and a body portion which, after filling, are welded together into a single indivisible unit (so sealing in and preventing subsequent access to the contents, and thus ensuring containment of the contents, whether powder, granular, liquid, gel or suspension presentations).

PVOH materials are particularly suited to thermal welding, a convenient variety of this technique being laser welding, though any suitable method can be used providing it does indeed make a permanent weld with the polymer used to form the capsule. Some other common methods are infra-red (IR), radio frequency (RF), and ultrasonic welding.

Some of these methods may require the addition of other items or processes to ensure their correct operation. For example, RF welding may require the use of a metal (normally aluminium) conductor in contact with the capsule surface. Laser welding will normally require the top surface to be transparent to the laser used, and the lower surface to be opaque to it. This can be achieved by avoiding opaque coatings and fillers on the outer surface of the capsule cap and by their application to the outer surface of the capsule body. For example, a circumferential line of a suitable material can be printed around the body at the required joining point to facilitate the weld at that point.

Of the various methods, the laser weld is preferred as there is no direct contact required, and it can achieve the very high production speeds required.

After placing the intended contents in the capsule body, and putting the cap on the body, the two portions of the capsule can be welded - by means of a laser beam,

say - into a single unit which cannot thereafter readily and without leaving visible traces be separated into body and cap in order to gain access to the contents. Accordingly, any attempt to tamper with the contents would be clearly obvious.

The two parts of the capsule that are to be welded together are made so that the open end of one will pass into the open end of the other with the smallest gap that can be practically achieved to allow easy assembly. Normally, but not necessarily, the capsule is designed with a stop on one or other component so that the entry of one into the other cannot overrun and stops at the same fixed position in every case.

The two halves or shells are in the closed position when the entire periphery of the open end of one is overlapped by the periphery of the open end of the other. The closed capsule is then ready for welding, and this is done by bringing the capsule into close proximity to the welding head. This distance will vary with the method of welding chosen. The welding equipment is operated, and forms a weld between the two layers in contact in the form of a line of weld in a closed loop around the periphery of the capsule. This can be achieved either by having the welding heads in the form of a ring (which may be continuous or made up of a number of discrete heads), or by rotating one or other of the capsule and the head around the other - say, by rolling the capsule past the head. The exact method will depend on the welding technology chosen.

It is also possible to use solvent welding - that is, using a solvent for the chosen injection-mouldable material so as to soften and render flowable the surface layers of the material where the two parts are in contact. In the PVOH case the solvent is conveniently

water or an aqueous electrolyte solution (typically containing an alkali metal halide such as lithium chloride as the electrolyte). This technique, however, requires another stage to the welding process, in which the solvent is applied to one of the surfaces to be in contact *before* the two shells are closed. This method is not preferred, however, as it is likely to be comparatively slow, and the addition of water and solute may well be detrimental to the ingredient(s) or other preparations contained within the capsule.

Due to the integrity of the welded seal, the capsule can be filled with any appropriate liquid, gel, or oil.

The invention provides a capsule made of a material that can be injection-moulded. The injection-moulding process allows controlled variations in the thickness of the walls and domed ends of either or both halves of the capsule, thereby allowing the release characteristics to be infinitely varied. The use of such moulded capsule shells permits the development of capsule formulations containing controlled-release beads or granules which can determine where the contents are released so that the system as a whole can be made to deliver its contents at the desired position, rate and period of release irrespective of differing physico-chemical properties of the contents.

In its broadest aspect this invention provides a capsular container made of a material that can be injection-moulded. This injection-moulding concept has several unexpected consequences, as does the choice of a polymer of the PVOH type for this purpose. Specifically, an injection-moulded container can be moulded in almost any shape that might be useful (as might have been

inferred from what has been said above). In particular, it can be given external raised (or lowered) areas

In another aspect, therefore, the invention provides a relatively large injection-moulded capsular container having raised portions moulded into its external surface.

The raised portions - for the most part they are referred to hereinafter as "raised", though obviously the effect of a raised part can be achieved by lowering the other parts - can be in the form of short, small pimple-like projections, or they can be ribs that extend wholly or partially either around or along the capsule. The portions may be designed to include or act as markings allowing identification of the capsule and its contents - either visually, by the sighted, or tactilely, by the visually-impaired, or even by a machine or reader. Thus, a code can be moulded into the surface so that a filled capsule can be identified at all stages of its life - by the manufacturer for quality assurance and quality control, by a wholesaler or retailer as part of a stock-control system, and by the User before utilisation, particularly those with vision impairment.

The surface of the capsule needs no pre-treatment prior to printing.

By suitable cutting of the moulds used, any required pattern can be moulded into the surface, either raised or incuse. Both raised and incuse variants bring different properties to the capsules, and the benefits of each are described hereinafter. The complexity of the pattern is limited only by the practical limitations on mould making.

The use of an incuse pattern has a number of interesting possibilities. For example, it can help determine the time of release of the container's

contents. Such an incuse pattern design may include a capsule of standard form but with relatively thick walls. Around the centre section of the capsule base is moulded an array of thin-walled incuse panels. Once the capsule has reached it's intended destination, the thin-walled panels in the capsule body quickly dissolve, leaving the capsule with a grid structure of holes. These holes can be small enough to prevent the internal contents leaving the capsule, but large enough to allow the dissolving medium to enter and make contact with the contents of the capsule. As has been described earlier, PVOH materials can, due to variations in molecular weight and extent of hydrolysis, be selected to dissolve at different speeds and at different temperatures in aqueous conditions. Hence, by varying the thickness and the dissolution characteristics of the injection-moulded capsule materials, the body of the capsule may be designed to dissolve or break up at a chosen rate.

Another possibility is to mould a capsule in a relatively sparingly-soluble polymer material - such as a high molecular weight PVOH having a high degree of hydrolysis - with a similar array of holes (rather than thin-walled soluble panels), and then in a separate process, after filling and capping, to cover the area containing the holes with a relatively soluble polymer either by spraying or by shrinking or gluing a soluble sleeve thereover. The relatively-sparingly soluble polymer used in this case could even be an insoluble polymer - provided, of course, that it is injection-mouldable.

Another consequence of using an injection-moulding method is that the mouldable material may easily include one or more additional substance that has some effect on

the way the capsule behaves in use - for instance, on its rate of dissolution.

Thus, in still another aspect the invention provides a relatively-large injection-moulded capsular container that is made from an injection-mouldable material that contains one or more particulate solid in order to accelerate the rate of dissolution of the container.

The simple dissolution of the solid in the chosen medium is sufficient to cause a significant acceleration in the container break-up, particularly so if a gas is also generated, when the physical agitation caused will result in the virtually immediate release of the contents from the container.

Such solids are of course subject to the same limitations of approval and compatibility as before. The most obvious solids for this purpose are the bicarbonate and carbonate salts of the alkali and alkaline-earth metals, typically sodium, potassium, magnesium and calcium.

The solid is very preferably extremely finely divided, typical particle sizes being in the range 1-25 micron, and preferably 5-10 micron.

Other materials that can be utilised to affect the capsule's dissolution rate are most preferably solid acidic substances with carboxylic or sulphonic acid groups or salts thereof. Substances suitable for this purpose are cinnamic acid, tartaric acid, mandelic acid, fumaric acid, maleic acid, malic acid, pamoic acid, citric acid, and naphthalene disulphonic acid, as free acids or as their alkali or alkaline-earth metal salts, with tartaric acid, citric acid, and cinnamic acid in the form of acids or their alkali metal salts being especially preferred.

One of the great practical problems of current hard gelatine capsules is their ability to hold a static electrical charge. Such capsules in production rapidly pick up a high static charge which has the effect of making them not only stick to each other and to all other non-polar surfaces but also making them attract particles of foreign material from their surroundings. It also means that the capsules are hard to fill, and that their surfaces must be treated immediately prior to printing. This phenomenon is common to some mouldable polymers, but not to PVOH, which is not only soluble, ingestible, mouldable and weldable, but in addition will not support a static charge capable of causing the problems described above. So, yet another consequence of using an injection-moulding method is that the mouldable material may be chosen having regard to its ability to pick up and retain a static charge - or may include one or more additional substance that has some effect on the way the capsule behaves in this respect.

Thus, in a still further aspect this invention provides a relatively-large injection-moulded capsular container being made from materials that will not hold a static charge.

The capsule of the invention is one that dissolves in the destined aqueous medium to release its contents therein. The term "dissolve" is used herein in a fairly general sense, to indicate that the capsule crumbles, decomposes, disintegrates or disperses; it need not actually dissolve, although in most cases it will.

Various embodiments of the invention are now described, though by way of illustration only, with reference to the following Examples (and Test Results) and also with reference to the accompanying diagrammatic Drawings in which:

<u>Figures 1A & B</u>	show longitudinal cross-sections of a capsular container of the invention in its open and closed states respectively;
<u>Figure 2</u>	shows the closed capsular container of Figure 1B but in see-through perspective;
<u>Figures 3A & B</u>	show longitudinal cross-sections of two- and three-compartment capsular containers of the invention;
<u>Figures 4A & B</u>	show respectively longitudinal and transverse cross-sections of another two-compartment capsular container of the invention;
<u>Figure 5</u>	shows a section through the wall of a solid-filled polymer capsule of the invention;
<u>Figures 6A-6</u>	show various different forms of moulding on and in the surface of capsular containers of the invention.

Figure 1 shows a two-part, one-compartment capsular container of the invention in its open and its closed form.

The body (11) and cap (12) are to be welded together, and are made so that the open end (11a) of one will pass into the open end (12a) of the other with the smallest gap that can be practically achieved to allow easy assembly. There is a "stop" - a ridge (11b) running all round outside of the body 11 that co-operates with a groove (12b) running all round the inside of the cap 12 - so that the entry of one into the other cannot overrun, and stops at the same fixed position in every case.

When the two halves or shells 11,12 are in the closed position (as in Figure 1B), with the entire periphery of the open end 11a of the body 11 overlapped by the periphery of the open end 12a of the cap 12, the capsular container is ready for welding. The welding equipment (not shown) forms a weld line (13) between the two layers all round the periphery of the container.

Figures 3 and 4 show different sorts of multi-compartment capsular container according to the invention.

In Figure 3 the container is made in two or more parts (three in Figure 3A, four are shown in Figure 3B, but there could be more) - in each case there is a single cap portion (32) and a plurality of body portions (as 31). The outer of the body portions 31 is much the same as an "ordinary" body portion (as in Figure 1), but each inner one is shaped at its "outer" end (as 31c) so that it will fit tightly *inside* the open mouth of the next body portion, much like in Figure 1 the body 11 fits inside the cap 12.

As shown (in Figure 3A), when the first (outer) body part 31 has been filled with product A, it may then be closed by the second (inner) body part 31 within it. That second body part 31 may then be filled with

product B, the cap 32 placed in position, and the three parts welded together at the same time.

Figure 4 shows a capsular container with body (41) and cap (42) two compartments side-by-side (Figure 4B shows a transverse section on the line A-A in Figure 4A). The two compartments can of course hold different products (A and B).

There is theoretically no limit to the number of separate chambers that can be produced either linearly (as in Figure 3) or side by side within the body portion (as in Figure 4). Of course, limitations will be set by practical problems of manufacture.

In Figure 5 there is shown a section through the wall of a solid-filled polymer capsular container of the invention.

Inert solids in powder form have been added to the polymer formulation prior to moulding. This provides a more rigid shell.

Figure 6 etc show various different forms of moulding on the surface of capsular containers of the invention, some in the form of cross-sections.

These are self-evident, and need little comment. Figure 6A,F, for example, shows a capsular container with longitudinal raised ribs, while Figure 6B shows one with lateral (or circumferential) raised ribs and Figure 6E shows one with helical ribs. Figure 6C,H shows a container with raised pimples, while Figure 6D,I shows one with raised identification coding patterns. Figures 6G,J,K,L and M show variants analogous to some of the others, but with *incuse* rather than raised portions.

Claims

1. A relatively-large capsular container that may be utilised for the delivery of some water-destined ingredient, which capsular container is made of a material that can be injection-moulded and will at least in part dissolve in the intended aqueous destination site, and wherein different parts of the container will take different times to dissolve.

2. A capsule as claimed in Claim 1, which has a body and cap each provided with a central axially-parallel partition, so that the capsule as a whole has two separate compartments, or which has three parts - a body, a first cap, and then a second cap to fit over the closed end of either the body or the first cap, so as also to result in a capsule with two separate compartments.

3. A capsule as claimed in either of the preceding Claims which is made of polyvinylalcohol.

4. A capsule as claimed in any of the preceding Claims, wherein the several parts are welded together.

5. A capsule as claimed in any of the preceding Claims, wherein the thickness of the walls and/or ends of the body and/or cap portions are adjusted during moulding to achieve the desired contents release characteristics.

6. A capsule as claimed in any of the preceding Claims, which capsule has relatively-raised portions moulded into its external surface.

7. A capsule as claimed in Claim 6, wherein the raised portions are in the form of short, small pimple-like projections, of ribs that extend wholly or partially either around or along the capsule, and/or of markings allowing identification of the capsule and its contents.

8. A capsule as claimed in either of Claims 6 and 7, wherein the relatively-raised portions provide an incuse pattern design on a capsule of standard form but with relatively thick walls, so forming an array of thin-walled incuse panels such that in use the thin-walled panels quickly dissolve, leaving the capsule with a grid structure of holes.

9. A capsule as claimed in any of Claims 6 to 8, which is moulded in a relatively sparingly-soluble, or even insoluble, polymer material with an array of holes, and then, after filling and capping the capsule, the area containing the holes is covered with a relatively soluble polymer.

10. A capsule as claimed in any of the preceding Claims, which capsule is made from an injection-mouldable material that contains one or more particulate solid in order to accelerate the rate of dissolution of the capsule.

11. A capsule as claimed in Claim 10, wherein the particulate solid has particle sizes in the range 5-10 micron.

12. A capsule as claimed in either of Claims 10 and 11, wherein the particulate sodium, potassium, magnesium or carbonate or bicarbonate, or is tartaric acid, citric acid, and cinnamic acid in the form of the acid or an alkali metal salt thereof.

13. A capsule as claimed in any of the preceding Claims, which capsule is made from materials that will not hold a static charge.

14. A capsule as claimed in any of the preceding Claims and substantially as described hereinbefore.

15. A method of making a capsule as claimed in any of the preceding Claims, which method is substantially as described hereinbefore.

The Patent Office

INVESTOR IN PEOPLE

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Application No: GB 0003304.3
Claims searched: 1-15

Examiner: Diane Davies
Date of search: 12 October 2000

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.R): B8C: CA; A5B

Int Cl (Ed.7): A61K 9/00, 9/20, 9/48; A61J 3/07

Other: Online databases: EPODOC, JAPIO, TXTE, WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X,	GB 2172803 A	(Standard Telephone Cables plc) Whole document: Water soluble capsules having walls with reduced thickness to give differential solubility	At least claim 1
X,	GB 2148235 A	(Warner-Lambert Co.) Whole document: injection moulding of capsules using polymers such as starch, see figures for capsules of varying thickness.	At least claim 1
X,	GB 1298084 A	(ERASME) Whole document: manufacture of capsules which are porous and use of PVA as a material for capsule manufacture by injection moulding - see page 1 lines 57, 74-5 & 85-6, page 2 line 119 to page 3 line 24 and Example 7.	At least claim 1
X	WO 9407470 A	(Pfizer) Whole document: pharmaceutical compositions having coatings of non-constant thickness and made of PVA	At least claim 1

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.